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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/667,494	09/23/2003	David W. Leung	077319-0381	8687

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/667,494	LEUNG ET AL.	
	Examiner	Art Unit	
	David J Steadman	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 23 September 2003 is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 9/23/03.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claim 1 is pending in the application.

[2] Applicants' amendment to the specification, filed September 23, 2003, is acknowledged.

[3] Receipt of an information disclosure statement (IDS), filed September 23, 2003, is acknowledged.

Information Disclosure Statement

[4] All references cited in the IDS filed September 23, 2003 have been considered by the examiner. A copy of Form PTO-1449 is attached to the instant Office action.

Priority

[5] Applicants' claim to domestic priority under 35 U.S.C. 121 to US non-provisional application 09/970,989, filed October 05, 2001, which issued as US Patent 6,670,143 and US non-provisional application 09/215,252, filed December 12, 1998, which issued as US Patent 6,300,487, is acknowledged. Applicants' claim to domestic priority under 35 U.S.C. 120 to US non-provisional application 08/618,651, filed March 19, 1996, which issued as US Patent 6,136,964 is acknowledged. While the examiner can find no support for the claimed polypeptide of SEQ ID NO:13 in the disclosure of application 08/618,651, the examiner can find support for the claimed polypeptide in the disclosures of applications 09/215,252 and 09/970,989.

Specification/Informalities

[6] Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120/121 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78) and *the status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No._____" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.*

[7] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: --Human Lysophosphatidic Acid Acyltransferase Gamma-1 Polypeptide--.

[8] The specification discloses sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have

not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). Applicants are requested to review the specification and identify those nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids by a proper sequence identifier.

Drawings

[9] The drawings disclose sequences that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). Applicants are requested to review the drawings and identify those nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids by a proper sequence identifier.

[10] The drawings are objected to because Figures 1-5 and 9-11 are not numbered in accordance with 37 CFR 1.84(u)(1), which states, "[p]artial views intended to form one complete view, on one or several sheets, must be identified by the same number followed by a capital letter." A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Claim Objections

[11] Claim 1 is objected to in the recitation of "LPAAT." Abbreviations, unless otherwise obvious, should not be recited in the claims without at least once reciting the entire phrase, i.e., "lysophosphatidic acid acyltransferase" for which the abbreviation is used. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[12] Claim(s) 1 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is confusing the in the recitation of "[a]n isolated polypeptide... ...comprising... ...SEQ ID NO:13 and enzymatically active fragments thereof." Based on the disclosure of the specification, it appears that the claimed invention is drawn to a single polypeptide that comprises SEQ ID NO:13. However, the wording of the claim indicates the claim is drawn to a polypeptide comprising SEQ ID NO:13 in addition to enzymatic fragments thereof. It is suggested that applicants clarify the meaning of the claim. In the interest of advancing prosecution, the claim has been interpreted as an

isolated polypeptide having LPAAT activity comprising SEQ ID NO:13 or an enzymatically active fragment of said polypeptide.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[13] Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention.

The claims are drawn to a genus of isolated polypeptides having LPAAT activity comprising SEQ ID NO:13 or an enzymatically active fragment thereof. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163

states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The specification discloses several representative examples of polypeptides having LPAAT activity and only a single representative species of the claimed genus of LPAAT polypeptides, *i.e.,* SEQ ID NO:13. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". MPEP 2111 directs the examiner to give claims their broadest reasonable interpretation. In this case, the specification indicates that the genus of claimed polypeptides is meant to encompass "fusion proteins such as those used to allow rapid purification of the polypeptide and *also can include hybrid polypeptides containing sequences from other proteins and polypeptides which are homologues of the inventive polypeptide*" (italics added for emphasis; p. 7, bottom). It should be noted that the specification fails to define those polypeptides that are considered to be "homologues of the inventive polypeptide." As such, the genus of "enzymatically active fragments thereof" encompasses a wide and variable genus including not only fragments of SEQ ID NO:13, but also fragments of a fusion protein comprising SEQ ID NO:13 and any protein that is considered to be a homologue thereof, broadly including fragments of any polypeptide having any catalytic activity. Thus, the disclosure of SEQ ID NO:13 is

insufficient to be representative of the attributes and features of *all* species encompassed by the recited genus of polypeptides comprising SEQ ID NO:13, including fusion proteins or enzymatically active fragments thereof. Given the lack of description of a representative number of ligands, linkers, and enzymes, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[14] Claim 1 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO:13, does not reasonably provide enablement for *all* enzymatically active fragments of a polypeptide comprising SEQ ID NO:13. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

It is the examiner's position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP §

2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

- The claims are overly broad in scope: The claims are so broad as to encompass all enzymatically active fragments of a polypeptide comprising SEQ ID NO:13, including enzymatically active fragments of a fusion protein comprising SEQ ID NO:13. As stated above, the specification indicates that the scope of claimed polypeptides is meant to encompass "fusion proteins such as those used to allow rapid purification of the polypeptide and also can include hybrid polypeptides containing sequences from other proteins and polypeptides which are homologues of the inventive polypeptide" (p. 7, bottom). It should be noted that the specification fails to define those polypeptides that are considered to be "homologues of the inventive polypeptide." As such, the scope of "enzymatically active fragments thereof" encompasses a broad scope of polypeptide fragments, including not only fragments of SEQ ID NO:13, but also fragments of a fusion protein *comprising* SEQ ID NO:13, *e.g.,* fusion moieties of a fusion protein comprising SEQ ID NO:13 having any structure and catalytic activity. The broad scope of claimed enzymatically active fragments is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of enzymatically active polypeptide fragments broadly encompassed by the claims. In this case the disclosure is limited to the polypeptide of SEQ ID NO:13.

- The lack of guidance and working examples: The specification fails to disclose even a single working example of an enzymatically active fragment of *any* polypeptide, including SEQ ID NO:15 and fails to provide guidance for making such fragments. For

example, even assuming *arguendo* the claim were limited to an enzymatically active fragment of SEQ ID NO:13, what amino acids of SEQ ID NO:13 are considered to be the active site of the enzyme such that deletion of "extraneous" amino acids – if any – would yield a fragment having LPAAT activity?

- The high level of unpredictability in the art: The ability of an enzyme to maintain the ability to catalyze a reaction is dependent upon numerous factors, including its three-dimensional fold. By removal of amino acids of a protein at its N- and/or C-termini, there is a high level of unpredictability as to whether the protein will maintain catalytic activity.

- The amount of experimentation required: It is not routine in the art to screen for all possible enzymatically fragments of any protein comprising SEQ ID NO:13 – including fusion proteins for all those fragments that are considered to be enzymatically active.

Thus, in view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability, and the significant amount of experimentation required, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. As such, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)).

Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

[15] Claim(s) 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. (US Patent Application Publication 2003/0049771 A1). The priority date relied upon for the reference of Baker et al. is October 29, 1998. Claim 1 is drawn to an isolated polypeptide having LPAAT activity, comprising the amino acid sequence of SEQ ID NO:13 or an enzymatically active fragment thereof. Baker et al. teach a polypeptide, SEQ ID NO:338 (Figure 338), that, absent evidence to the contrary, comprises an enzymatically active fragment of SEQ ID NO:13 (see Appendix A). This anticipates claim 1 as written.

Conclusion

[16] Status of the claims:

- Claim 1 is pending.
- Claim 1 is rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (571) 272-0942. The Examiner can normally be reached Monday-Thursday and alternate Fridays from 7:30 am to 5:00 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (571) 272-0928. The FAX number for submission of official papers to Group 1600 is (703) 872-9306. Draft or informal FAX communications should be directed to (571) 273-0942. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

12-08-04

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1652